REMARKS

Claims 1-7, 15-28, 31 and 34-41 are pending in the instant application. Claims 1-7, 15-28, 31 and 34-41 have been rejected. Claims 2, 3, 4, 5, 6, 7, 19, 20, 21, 28, 31, 35, 37, 38, 39, 40 and 41 have been amended. Support for these amendments is provided in the specification at pages 14, lines 11-26 and page 15, lines 15-18. Thus, no new matter has been added. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Proposed Drawing Correction

The drawings have been objected to. Specifically, Figures 3-10 and 13 are suggested to have unacceptable top and left margins. Further, Figures 1-14 are suggested to have poor line quality and numbers and reference characters that are not plain and legible. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are submitting herewith corrected drawings with acceptable line quality, plain and legible numbers and reference characters and that comply with the margin requirements. Acceptance of these drawings, as they are the highest quality obtainable at this time, is respectfully requested. No new matter is added by these replacement drawings

and entry is respectfully requested.

II. Information Disclosure Statement

The listing of the references in the specification was in no way intended by Applicants to serve as an Information Disclosure Statement. Applicants submitted a separate Information Disclosure Statement which complied with 37 C.F.R. 1.98 which was considered by the Examiner before the first Office Action as indicated by the Examiner's initialing on December 27, 2002.

III. Rejection of Claims 1-7, 16-28, 31 and 34-41 under 35 U.S.C. § 112, first paragraph

Claims 1-7, 15-28, 31 and 34-41 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner has acknowledged the specification to be enabling for Mab monoclonal antibodies 8I-7 and 2I-14. However, the Examiner suggests that the specification does not reasonably provide enablement for any compound that specifically binds a myofilament protein modification product. Further, the Examiner suggests that the written description in this case only sets forth Mab monoclonal antibodies 8I-7 and 2I-14 and therefore is not commensurate in scope with the claims drawn to any compound that specifically binds the myofilament protein modification product.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that the pending claims require antibody binding to practice the method. Pending claims are drawn to evaluating for the presence or absence of one or more different myofilament protein modification products in a biological sample. While antibody binding is one method of evaluating for the presence of a myofilament protein modification product, other methods for evaluating for the presence of a myofilament protein modification product are taught and/or exemplified to be effective in the instant application. For example, selection and use of peptides or peptidomimetics which specifically recognize and bind a myofilament protein modification product is taught at page 24, lines 10-23 of the instant specification and direct detection of myofilament protein modification product(s) using, for example HPLC and molecular sieve techniques, is taught at page 25, line 29 through page 26, line 2. Further, an example of HPLC analysis to directly detect myofilament proteins and modification products thereof is set forth at page 35, line 10 through line 29.

Further, contrary to the Examiner's suggestion that the instant application only sets forth or teaches mAbs 8I-7 and 2I-

14, multiple antibodies and methods for their use in detecting the myofilament proteins and modification products thereof, and in particular chemical adducts of myofilament proteins, degradation products and complexes thereof which are indicative of muscle damage are taught. The Examiner is respectfully directed to page 33-34 of the instant application wherein the following antibodies are taught:

mAb anti-TnT clone JLT-12 (Sigma Chemical Co. St. Louis, MO)

mAb anti-α-actinin clone EA-53 (Sigma Chemical Co. St. Louis, MO)

mAb anti-α-actinin clone 157 (Spectral Diagnostics, Toronto, CA)

mAb anti-MLC1 (Abbott Laboratories, Chicago, IL)

anti-sarcomeric actin (Sigma Chemical Co. St. Louis, MO)

anti-glyceraldehyde phosphate dehydrogenase (Cedarline Lab. Ltd, Canada)

P1, anti-peptide antibody to residue 1-26 of cTnI (Biospacific, Inc.)

P3, anti-peptide antibody to residues 26-56 of human cTnI (Biospacific, Inc.)

anti-TnI 10F2 (MAb 10F2; Research Diagnostics, Flanders, NS)

anti-TnI mAb 3I-35 (Spectral Diagnostics, Toronto, CA)

anti-TnI mAb C5 (Research Diagnostics, Flanders, NS) Additional antibodies are taught in Example II at page 36, lines 19 through 25 and Example III at page 42, lines 7 through 14.

Thus, the instant specification clearly provides sufficient guidance with respect to multiple methods for evaluating for the presence of a myofilament protein modification product so that one of skill in the art can make and use the invention commensurate in scope with the claims. Accordingly, the instant specification meets the enablement requirements of 35 U.S.C. § 112, first paragraph.

Further, the written description sets forth sufficient detail with respect to a multitude of antibodies as well as other compounds and methods for evaluating for the presence of a myofilament protein modification product so that one of skill would recognize the inventor to be in possession of the invention claimed. Such detailed teachings also clearly place the public in possession of the invention as claimed. Thus, the specification also meets the objectives of the written description requirements of 35 U.S.C. § 112, first paragraph. See MPEP 2163(I).

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement and written description is

therefore respectfully requested.

IV. Double Patenting Obviousness-type Rejection

Claims 1-7, 15-28, 31 and 34-41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 09/115,589. The Examiner has acknowledged that the conflicting claims are not identical. However, the Examiner suggests that the invention is encompassed in the claims of application number 09/115,589 wherein the claims read on any myofilament protein modification product.

As acknowledged by the Examiner in this rejection, both applications are still pending and may undergo further claim amendments that render moot this obviousness-type double patenting rejection. It is therefore respectfully requested that this rejection be held in abeyance until one of these applications has been acknowledged to be in condition for allowance. If at that time the obviousness-type double patenting issue still exists, Applicants will file the appropriate terminal disclaimer(s).

V. Provisional Rejection of Claims 1-7, 15-28, 31 and 34-41 under 35 U.S.C. § 103(a)

Claims 1-7, 15-28, 31 and 34-41 have been provisionally rejected under 35 U.S.C. § 103(a) as being obvious over copending Application No. 09/115,589.

The corresponding Canadian Patent Application Number 2,243,372 was published on or around January 16, 1999. Applicants are providing herewith a Supplemental Information Disclosure Statement and the requisite fee to enter this Canadian Patent Application into the record of the instant application.

As acknowledged by the Examiner, these applications have a common inventor, Dr. Jennifer Van Eyk. Applicants are submitting a Declaration by Dr. Van Eyk herewith which states that any invention disclosed, but not claimed in the copending application was derived from her work and thus is not an invention "by another". Accordingly, neither the copending U.S. Application nor the published Canadian Patent Application are "by another" and therefore they are not valid prior art references with respect to the instant application.

Withdrawal of this rejection under 35 U.S.C. §103(a) is

therefore respectfully requested.

VI. Rejection of Claims 1, 15-16, 19-21 and 34-37 under 35 U.S.C. 102(b)

Claims 1, 15-16, 19-21 and 34-37 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wicks et al. (WO 94/27156). The Examiner suggests that Wicks et al. measure troponin I in a complex sandwich assay having immobilized solid phases for the purpose of assaying irreversible cardiac damage from biological samples such as blood. It is the Examiner's opinion that TnI is a protein meeting the limitations of a myofilament protein modification product being a chemical adduct of a myofilament protein.

Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's suggestion that TnI detected by Wicks is a protein meeting the limitations of a myofilament protein modification product being a chemical adduct of a myofilament protein. The definition for the term chemical adduct is provided in the specification at page 14, lines 11-26. This term "chemical adducts" is defined as "a peptide species formed by bonding, for example covalent bonding, of a polypeptide or a polypeptide fragment and a *different*

compound". Specifically excluded from this definition are covalent linkages of two similar species, i.e. protein-protein complexes. See page 14, lines 13-14. A chemical adduct which is the linkage of a **different** chemical compound or moiety to a protein-protein complex or protein degradation product is encompassed by this definition by this definition of chemical adduct. See page 14, lines 15-17.

Wicks et al. measure troponin I in a complex sandwich assay. The binding partners used are capable of binding troponin I and the C subunit of the troponin complex. Nowhere do Wicks et al. teach detection of a chemical adduct of troponin I wherein troponin I is bound to a *different* compound other than covalent linkage to another protein, as being indicative of muscle damage. Accordingly, since this reference does not teach all the elements of the claimed invention, its teachings cannot anticipate the claimed invention. See MPEP § 2131.

In an earnest effort to clarify distinctions of the present invention from prior art teachings such as Wicks et al. wherein detection of a chemical adduct of a myofilament protein was **not** performed, Applicants have amended the claims to more clearly state that a chemical adduct of a myofilament protein is being

detected. Support for this amendment is provided in the specification at page 14, lines 11 through 26 and page 15, lines 15-18.

Withdrawal of this rejection under 35 U.S.C. § 102(b) is respectfully requested in light of the above remarks and the amendments to the claims.

VII. Rejection of Claims 2-7, 11-14, 17-18, 22-28, 31 and 38-41 under 35 U.S.C. § 103(a)

Claims 2-5, 7 and 38-40 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Wicks et al. (WO 94/27156) in view of Wicks et al. (U.S. Patent 5,834,220). The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to measure two different myofilament protein degradation products (troponin I and troponin C) in muscle damage as taught by Wicks et al. in the method of Wicks et al. (WO 94/27156) involving troponin I analysis because Wicks et al. taught that troponin I is one of three subunits of the troponin complex. The Examiner suggests that one of skill would have been motivated to do this to acquire the enhanced sensitivity and ability to reduce false positives while providing more data sets for analysis, wherein accurate and

precise detection is available.

Claims 6, 11-14, 17-18, 22-28, 31 and 41 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Wicks et al. (WO 94/27156) in view of Wicks et al. (U.S. Patent 5,834,220) and further in view of Van Eyk et al. (U.S. Patent 6,248,549). The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to measure two different myofilament protein degradation products from different proteins with respect to their phosphorylation states (troponin I and calponin) in muscle damage as taught by Van Eyk et al. in the method of Wicks et al. (WO 94/27156) in view of Wicks et al. to detect troponin I analysis because Van Eyk et al. taught that such method configuration allowed for the assessment of compositions in a screening format for their effect on PAK kinase activity or expression with respect to muscle disorders.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's characterization of the method of Wicks et al. for detecting troponin I as a method for detecting myofilament protein degradation products. Degradation product, as defined in the instant specification at page 14, line 27, is any **fragment** of

a myofilament protein. Intact TnI, as detected by Wicks et al. is not a fragment of a myofilament protein and therefore is not a degradation product in accordance with the instant invention.

Further, as discussed in Section VI, *supra*, claims of the instant application are drawn to detecting a **chemical adduct** of a myofilament protein, which is defined in the application as "a peptide species formed by bonding, for example covalent bonding, of a polypeptide or a polypeptide fragment and a *different* compound". Specifically excluded from this definition are covalent linkages of two similar species, i.e. protein-protein complexes. See page 14, lines 13-14. A chemical adduct which is the linkage of a different chemical compound or moiety to a protein-protein complex or protein degradation product is encompassed by this definition by this definition of chemical adduct. See page 14, lines 15-17. Neither Wicks et al. (WO 94/27156), Wicks et al. (U.S. Patent 5,834,220) nor Van Eyk et al. (U.S. Patent 6,248,549). teach or suggest detecting a chemical adduct of a myofilament protein to diagnose muscle damage.

Accordingly, the combination of cited references fails to provide the requisite teaching or suggestion of all claim

limitations to render obvious a claim drawn to a method for assessing muscle damage by evaluating for the presence or absence of one or more chemical adducts of a myofilament protein in the biological sample. See MPEP § 2143.

Withdrawal of these rejections under 35 U.S.C. § 103(a) is therefore respectfully requested.

VIII. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Kathleen A. Tyrrell
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Date: **December 23, 2003**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**PTQ-0028**
Inventors:	**Van Eyk et al.**
Serial No.:	**09/419,901**
Filing Date:	**October 18, 1999**
Examiner:	**Cook, Lisa V.**
Group Art Unit:	**1641**
Title:	**Methods of Diagnosing Muscle Damage**

Dear Sir:

DECLARATION BY JENNIFER VAN EYK

I, Jennifer Van Eyk hereby declare:

1. I am a co-inventor on the above-referenced patent application with Ralf Labugger and Irina Neverova and am familiar with the conception and reduction to practice of the claimed invention.

2. I am also a co-inventor of U.S. Patent Application Serial No. 09/115,589 filed July 15, 1998 naming Steven Iscoe, Jeremy Simpson and myself as co-inventors. Any inventions disclosed, but not claimed in this copending application, were derived from my work.

I hereby declare that all statements herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both, under §1001 of Title 18 of the United States code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.

Jennifer Van Eyk

Jennifer Van Eyk

11/26/2003

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